

GenCore version 5.1.6
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OM protein - protein search, using sw model

Run on: April 13, 2005, 08:39:07 ; Search time 66.0833 Seconds
(without alignments)
228.252 Million cell updates/sec

Title: US-10-616-410-2_COPY_5_43

Perfect score: 215
Sequence: 1 EKLPPGWEKMRSSRRVYFNHITNASQWERPSGSSS 39

Scoring table: BLOSUM62

Gapop 10.0 , Gapext 0.5

Searched: 2105692 seqs, 386760381 residues

Total number of hits satisfying chosen parameters: 2105692

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : A_Geneseq_16Dec04: *
1: Geneseqp1980s: *
2: Geneseqp1990s: *
3: Geneseqp2000s: *
4: Geneseqp2001s: *
5: Geneseqp2002s: *
6: Geneseqp2003as: *
7: Geneseqp2003bs: *
8: Geneseqp2004s: *

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	Query Match	Length	DB ID	Description
1	215	100.0	39	3	AAB21975 Pini/huma
2	215	100.0	163	2	AAW18312 NIMA-inte
3	215	100.0	163	2	AAV48377 Human pro
4	215	100.0	163	4	AGG66532 Human int
5	215	100.0	163	7	ADG72366 Human pet
6	215	100.0	163	7	ADG65051 Pini prot
7	215	100.0	163	8	ADR30820 Bovine pin
8	211	98.1	87	4	AAB87657 Bovine me
9	211	98.1	145	7	ADM05756 Human pro
10	209	97.2	163	7	ADG65052 Pini R14A
11	198	92.1	141	8	ADP29953 Human sec
12	191	88.8	34	4	AAB74938 Peptidyl
13	175	81.4	195	4	AAB32052 Novel hum
14	175	81.4	259	4	ABG11947 Novel hum
15	172	80.0	31	3	AAB21943 Pini/huma
16	169	78.6	191	4	ABG12572 Novel hum
17	127	59.1	70	4	ABB43821 Peptide #
18	127	59.1	70	4	AAM37729 Peptide #
19	127	59.1	70	4	AAM77544 Human bon
20	127	59.1	70	4	AAM64786 Human bra
21	127	59.1	70	5	ABG46568 Human pep
22	116	54.0	166	4	ABG66150 Drosophil
23	112	52.1	37	5	AAB87969 Human WW
24	112	52.1	870	4	AAB05495 Human ubi
25	112	52.1	870	6	AAB32722 Nedd-4-1i

26	112	52.1	870	8	ADQ19348 Human sof
27	112	52.1	870	8	ABM81770 Tumour-as
28	112	52.1	906	2	AAW36795 Novel hum
29	112	52.1	906	7	ADB49242 Novel hum
30	111.5	51.9	335	7	ADC64238 Human SMU
31	111.5	51.9	748	2	AAW13384 Human pro
32	111.5	51.9	748	4	AAAB31477 Amino aci
33	111.5	51.9	748	7	ADN95750 Human BRC
34	111.5	51.9	804	4	AAU19610 Human dia
35	111.5	51.9	831	8	ADN05464 Antipsoori
36	109.5	50.9	37	2	AAW37638 Peptide c
37	109.5	50.9	38	7	ADB49230 Novel hum
38	109.5	50.9	474	2	AAAY10943 Amino aci
39	109.5	50.9	474	7	ADB47966 Novel hum
40	109.5	50.9	474	8	ADJ55521 Novel hum
41	109.5	50.9	739	4	ABG16477 Novel hum
42	109.5	50.9	739	4	ABG68173 Atrophin-
43	109.5	50.9	739	6	AAE32720 Atrophin-
44	109.5	50.9	739	6	ABR41097 Human atr
45	109.5	50.9	739	7	ADB98717 Human atr

ALIGNMENTS

RESULT 1
AAB21975
ID AAB21975 standard; peptide; 39 AA.

XX AC AAB21975;

XX DT 02-JAN-2001 (first entry)

XX DE Pini/human peptide containing a WW-domain #2.

XX KW WW-domain; protein-protein interaction; cell growth regulation;
XX KW protein degradation regulation; Alzheimer's; Dementia pugilistica;
XX KW Down's syndrome; Parkinson's disease; Pick's; neurodegenerative;
XX KW microtubule assembly; tau; hyperplasia; neoplasia; malignancy; psoriasis;
XX KW retinosis; atherosclerosis; leukaemia; lymphoma; papilloma;
XX KW pulmonary fibrosis; rheumatoid arthritis; multiple sclerosis;
XX KW muscular dystrophy; human.

XX OS Homo sapiens.

XX PN WO200048621-A2.

XX PD 24-AUG-2000

XX PF 18-FEB-2000; 2000WO-US004278.

XX PR 18-FEB-1999; 99US-00252404.

XX PA (BETH-) BETH ISRAEL DEACONESS MEDICAL CENT.

XX PI Lu KP, Zhou XZ;

XX DR WPI; 2000-594014/56.

XX PT Mediating protein-protein interactions, useful for regulating cell growth and for treating neurodegenerative disorders, comprises modulating binding of WW domain containing polypeptide with phosphorylated ligand.

XX PS Disclosure; Fig 6; 82pp; English.

XX CC The present invention relates to a method for mediating protein-protein interaction, which comprises modulating the binding of a WW-domain containing peptide with a phosphorylated ligand e.g. tau. WW-domains are highly conserved regions of approximately 40 amino acid residues with two invariant tryptophans (W) in a triple stranded beta-sheet. The present sequence is one such WW-domain. When a WW-domain containing peptide is phosphorylated at serine or threonine residues, dephosphorylation of ligands bound to the peptide is inhibited. The present peptide may be

Exhibit B

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useful for mediating protein-protein interaction, regulating cell growth, regulating protein degradation, restoring the function of tau to bind microtubules and promote or restore microtubule assembly in neurodegenerative diseases e.g. Alzheimer's, Dementia pugilistica, Down's syndrome, Parkinson's disease, Pick's disease, Multiple sclerosis, myotonic dystrophy, Niemann-Pick disease, prion disease with tangles, Myotonic dystrophy, Niemann-Pick disease, prion disease with tangles, progressive supranuclear palsy and subacute sclerosing panencephalitis. In addition, inhibitors or stimulators of interactions between WW-domains and ligands of the present invention can be used to treat hyperplastic and neoplastic disorders e.g. all forms of malignancies, psoriasis, retinosis, atherosclerosis resulting from plaque formation, leukaemias, benign tumour growth, lymphomas, papilomas, pulmonary fibrosis and rheumatoid arthritis

Sequence 39 AA;
Query Match 100.0%; Score 215; DB 3; Length 39;
Best Local Similarity 100.0%; Pred. No. 5.7e-22;
Matches 39; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
OY 1 EKLPPGWEKMRSSGRVYFNHITNASOWERPSGNSSS 39
DB 1 EKLPPGWEKMRSSGRVYFNHITNASOWERPSGNSSS 39

RESULT 2
AAW18312
ID AAW18312 standard; protein; 163 AA.
XX
AC AAW18312;
XX
DT 09-DEC-1997 (first entry)
XX
DE NIMA-interacting protein Pin1.
XX
KW Pin1; protein interacting with NIMA; cell proliferation; mitosis;
KW peptidyl-propyl cis/trans isomerase; adenocarcinoma; cancer; leukaemia;
KW psoriasis; pemphigus vulgaris; rheumatoid arthritis;
KW acute respiratory distress syndrome; septic shock; inflammation; therapy.
XX
OS Homo sapiens.

Key Location/Qualifiers
Domain 4..43
/label= WW
/note= "conserved tryptophan domain thought to be mediate protein-protein interactions"
Peptide 54..69
/note= "putative nuclear localisation signal"
Domain 59..163
/label= PPI
/note= "peptidyl-propyl cis/trans isomerase domain"

WO9717986-A1.
XX
XX
XX 22-MAY-1997.
XX
XX 28-OCT-1996; 96WO-US017334.
XX
XX 13-NOV-1995; 95US-00555912.
XX
XX (SALK) SALK INST BIOLOGICAL STUDIES.
XX
XX Hunter T, Lu KP;
PI WPI; 1997-289057/26.
DR N-PSDB; AAT68888.
XX
XX Protein, Pin1, interacting with NIMA - used for treating cell proliferative disorders.

XX This human polypeptide sequence comprises Pin1, an 18 kDa protein that has peptidyl-propyl cis/trans isomerase activity, associates with NIMA protein kinase, inhibits the mitosis-promoting function of NIMA when overexpressed, and induces mitotic arrest and nuclear fragmentation when depleted. Its sequence was deduced from a DNA sequence (AAT68888) identified in an HeLa library using a yeast two-hybrid system. A recombinant expression vector comprising the DNA sequence and host cells containing the vector are claimed. Methods are also claimed for identifying proteins that inhibit the mitosis promoting function of NIMA protein kinase and for controlling the growth of a cell by reducing Pin1 activity or Pin1 expression using an inhibitor, anti-Pin1 antibody, antisense nucleotide sequence or ribozyme, or by increasing Pin1 activity in the presence of an activator or increasing Pin1 expression using an enhancer. This allows treatment of cell proliferation disorders such as adenocarcinomas, cancers, psoriasis, pemphigus vulgaris, acute respiratory distress syndrome, rheumatoid arthritis, septic shock and inflammation

Sequence 163 AA;
Query Match 100.0%; Score 215; DB 2; Length 163;
Best Local Similarity 100.0%; Pred. No. 3.1e-21;
Matches 39; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
OY 1 EKLPPGWEKMRSSGRVYFNHITNASOWERPSGNSSS 163
DB 1 EKLPPGWEKMRSSGRVYFNHITNASOWERPSGNSSS 163

RESULT 3
AAY48377
ID AAY48377 standard; protein; 163 AA.
XX
AC AAY48377;
XX
DT 08-DEC-1999 (first entry)
XX
DE Human prostate cancer-associated protein 74.
XX
KW Expressed sequence tag; EST; prostate; tumor; treatment; gene therapy;
KW cancer; tissue specificity; human.

Homo sapiens.
XX
XX DE19811194-A1.
XX
XX 16-SEP-1999.
XX
XX 10-MAR-1998; 98DE-01011194.
XX
XX 10-MAR-1998; 98DE-01011194.
XX
XX (META-) METAGEN GES GENOMFORSCHUNG MBH.
XX
XX Specht T, Hinzmann B, Schmitt A, Pilarsky C, Dahl E, Rosenthal A;
XX
XX N-PSDB; AAZ33510.
XX
XX WPI; 1999-519629/44.

New nucleic acid expressed at high level in normal prostatic tissue and encoded polypeptides, used to treat cancer and screen for therapeutic agents.
XX
XX Claim 25; 152; 194pp; German.
XX
XX This invention describes novel nucleic acid sequences (A) that are expressed at high level in normal prostatic tissue. Polypeptides (I) encoded by (A) are used: (a) for identifying agents for treatment of prostatic cancer and (b) for therapy of prostate cancer, optionally where expressed by gene therapy methods. (A) is also used to isolate full-length genes (for gene therapy) and for recombinant production of (I), which can be used to raise specific antibodies. (A) are identified by